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Docket No. A-67824-1/AJT

Anticipated Classification of this Application:

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Prior Application: 09/454,273

Examiner: not assigned

Art Unit: 2878

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DATE OF DEPOSIT November 16, 2000
I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO: BOX PATENT APPLICATION FEE, ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231.

TYPED NAME KARI BATEMAN

SIGNED

Box PATENT APPLICATION FEE
Assistant Commissioner for Patents
Washington, DC 20231

Sir:

This is a request for filing a Continuation-in-part application under 37 C.F.R. 1.53(b), in the name of Keqi Tang, Alan E. Schoen, Jean-Jacques Dunyach, for MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION. This continuation-in-part claims priority to pending application Serial No. 09/454,273 filed on December 3, 1999.

1. Enclosed is a continuation-in-part application.

2. Enclosed is a new Declaration (unsigned).

3. The filing fee is calculated below:

Claims as filed in the prior application, less any claims canceled by amendment below:

	(Col. 1)	(Col. 2)	SMALL ENTITY			OTHER THAN A SMALL ENTITY	
FOR:	NO. FILED	NO. EXTRA	RATE	FEE	OR	RATE	FEE
BASIC FEE				$355	OR		$710
TOTAL CLAIMS	10 -20 =	0	x 9 =	$___	OR	x 18 =	$___
INDEP CLAIMS	4 -3 =	1	x 40 =	$___	OR	x 80 =	$ 80
[ ] MULTIPLE DEPENDENT CLAIM PRESENTED			+135 =	$___	OR	+270 =	$270
*If the difference in Col. 1 is less than zero, enter "0" in Col. 2.			TOTAL	$___	OR	TOTAL	$1060

4. The Commissioner is hereby authorized to charge any additional fees which may be required, including extension fees, or credit any overpayment to Deposit Account No. 06-1300 (Order No. A-67824-1/AJT).

5. Our check in the amount of $1,060.00 is enclosed.

6. Informal drawings are enclosed, 8 sheets.

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MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION

Related Applications

This application claims priority to pending application serial no. 09/454,273 filed December 3, 1999.

Field of the Invention

This invention relates generally to mass spectrometry, and more particularly to mass spectrometers employing atmospheric pressure ion sources such as electrospray or atmospheric pressure chemical ionization. More particularly, the invention relates to the use of two consecutive ion guides between the ion source and the mass analyzer to dissociate adduct ions, thus increasing the ion current for the analytically useful molecular species.

Background of the Invention

Generally, the interface between the atmospheric pressure ion source and the mass analyzer includes a capillary tube or other restrictive aperture which determines ion and gas throughput between the atmospheric pressure ionization region and a lower pressure region. The ions are drawn through the capillary or other restrictive aperture and directed to a downstream conical skimmer with a small aperture through which the sample ions flow. A tube lens or other electrostatic or electrodynamic focusing element may be associated with the capillary to force ions to the center of the jet stream leaving the capillary to thereby increase the ion transmission through the aperture of the skimmer. Reference is made to U.S. Patent No. 5,157,260 which

describes the operation of an atmospheric pressure ionization source, capillary lens and conical skimmer. One or more vacuum stages are interposed between the skimmer and the mass analyzer which is operated at vacuum pressures in the free molecular flow region.

The prior art interface vacuum stages have included ion guides to transfer the ions through the stages of decreasing pressure into the mass analyzer. In many prior art systems, the ions are guided by electrostatic lenses. In other systems, the ions are guided by electrodynamic multipole ion guides.

The use of an r.f.-only octopole ion guide for focusing and guiding ion beams has been described by Teloy and Gerlich (Chem. Phys., Vol. 4, p. 417, 1974) and Jarrold et. al. (Mol. Phys., Vol. 39, p. 787, 1980).

The dissociation of mass-selected ions in an r.f.-only quadrupole by collision with a target gas at low translational energies (E_{lab} < about 100 eV) has been described by R. A. Yost and C. G. Enke et. al. (Anal. Chem., Vol. 51, p. 1251a, 1979), and Dawson et. al. (Int. J. Mass Spec. Ion Proc., Vol. 42, p. 195, 1982).

McIver et. al. described the use of an r.f.-only quadrupole ion guide for guiding a beam of mass-selected ions into a Fourier-transform ion cyclotron resonance mass analyzer (Int. J. Mass Spec. Ion Proc., Vol. 64, p. 67, 1985).

Szabo described the theory of operation for multipole ion guides with various electrode structures (Int. J. Mass Spec. Ion Proc., Vol. 73, pp. 197-312, 1986).

Efficient transport of ions through vacuum chambers by multipole ion guides has been described by Smith et. al. (Anal. Chem., Vol. 60, pp. 436-441, 1988).

Beu et. al. described the use of three quadrupole ion guides to transport ions from an atmospheric pressure ionization source through three vacuum pumping stages into a Fourier-transform ion cyclotron resonance mass analyzer (J. Am. Soc. Mass Spec., Vol. 4, pp. 557-565, 1993).

U.S. Patent No. 4,963,736 describes the use of a multipole ion guide in the first pumping stage of a two-stage system. Operation of the multipole ion guide in certain length-times-pressure regimes is claimed for the purposes of enhancing ion signal.

U.S. Patent No's. 5,179,278 and 5,811,800 describe the temporary storage of ions in an rf multipole rod system for subsequent analysis in an r.f. quadrupole ion trap mass spectrometer. This is done for the purpose of matching the time scales of

compounds eluting from chromatographic or electrophoretic separation devices to the time scale of mass spectrometric analyses performed by an r.f. quadrupole ion trap.

U.S. Patent No. 5,432,343 describes an ion focusing lensing system for interfacing an atmospheric pressure ionization source to a mass spectrometer. It describes the use of an electrostatic lens in a transition flow pressure region of the interface, claiming benefit of independent adjustment of operating voltages controlling the collisionally induced dissociation and declustering processes. Enhancement of ion beam transmission into the mass analyzer is also claimed.

U.S. Patent No. 5,652,427 describes in one embodiment a system in which a multipole ion guide extends between two vacuum stages and in another embodiment a system which includes a multipole in each of two adjacent stages. Improved performance and lower cost are claimed.

U.S. Patent No. 5,852,294 describes the construction of a miniature multipole ion guide assembly.

A goal to be achieved in all single or multiple interface vacuum chambers is to transport as many protonated molecular cations or molecular anions as possible from the atmospheric pressure ionization source to the mass analyzer. However, many solvent adduct ions which are formed in the high pressure region travel through the interface vacuum chambers into the analyzer. The process of solvent adduction in the mass spectrometer system is generally considered to be a non-covalent association between sample ions of interest and neutral solvent molecules. Thus, in the case of introduction of an analyte into an electrospray or atmospheric pressure chemical ionization source, the ion current produced from that analyte may be divided between the protonated molecular cation or molecular anion and one or more solvent adduct species. Specific detection is usually accomplished by monitoring the ion signal, or derivative of that signal, for one specific mass. In the case where solvent adducts are formed, the limit of detection or limit of quantitation for the analyte is reduced.

Experimental evidence indicates that these adduct ions are predominantly formed in the high pressure regions of the system ranging from the API source region through the interface vacuum regions. The degree of adduction varies directly with the pressures in these regions. The formation of adduct ions significantly reduces the abundance of sample analyte ions. Furthermore, the adduct ions which enter into the

mass analyzer complicates the mass spectrum and make the identification of mass peaks more difficult.

Objects and Summary of the Invention

It is an object of the present invention to provide a mass spectrometer system employing an ion source with multiple ion guides configured and operated to convert adduct ions into sample ions and a method of operating multiple ion guides to convert adduct ions into sample ions to thereby increase the analyte ions current and sensitivity of the mass spectrometer system.

In accordance with the invention, there is provided a mass spectrometer including a mass analyzer disposed in a high vacuum chamber for analyzing ions formed in an ionization source which includes first and second evacuated interface chambers immediately preceding the mass analyzer chamber, with the first interface chamber being at a higher pressure than the second interface chamber, and including a first ion guide for guiding ions from the ion source into said second interface chamber which includes a second multipole ion guide for guiding the ions from the first interface chamber into the high vacuum analyzer chamber for analysis. Both r.f. and DC potentials are applied to the said first and second ion guides to ensure ion focusing and transmission through related vacuum chamber. A first ion lens is disposed at the input of the first interface chamber for directing ions into the first multipole ion guide, an interchamber ion lens is disposed between the first and second interface chambers for directing ions into said second multipole ion guide, and an ion lens or a lens stack is disposed between the second interface chamber and the analyzer chamber for directing ions into said analyzer for analysis. These ion lenses also serve as gas conductance restrictors between said interface chambers.

A DC voltage source is connected to provide a potential difference between the first lens and the first multipole ion guide or between interchamber lens and the second multipole ion guide or both which defines the ion's translational kinetic energy as it enters the second multipole ion guide. The ion's translational kinetic energy is chosen such that at the vacuum pressure of the second interface chamber adduct ions are converted into sample ions by collision induced dissociation without fragmentation of sample ions whereby the sample ion current entering the analyzer is increased, thereby increasing the sensitivity of the mass spectrometer system.

There is provided a method of mass analyzing ions produced in an atmospheric pressure ionization source in which adduct ions formed in the mass spectrometer system are dissociated prior to analysis to increase the analyte ion current to the mass analyzer and the sensitivity of the mass spectrometer system.

There is provided a method of operating a mass spectrometer system in which an analyzer in a vacuum chamber analyzes ions formed in an atmospheric pressure ionization source. The system includes first and second multipole ion guides disposed in serial first and second evacuated chambers immediately preceding the analyzer. The method comprises applying a DC voltage between the ion lens preceding either the first or the second multipole ion guide to provide translational kinetic energy to the adduct ions sufficient to dissociate any adduct ions at the pressure of the second chamber without fragmenting the sample ions whereby to increase the sample ion current directed into the analyzer and the sensitivity of the mass spectrometer system.

Brief Description of the Drawings

The foregoing and other objects of the invention will be more clearly understood from the following description when read in conjunction with the accompanying drawings in which:

Figure 1 is a schematic view of a mass spectrometer system including an atmospheric pressure ion source coupled to a tandem mass analyzer through evacuated interface chambers with multipole ion guides.

Figures 2A and 2B show the mass spectra for an injection of Alprazolam in a liquid stream flowing at 400 microliters per minute (µl/min) with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 3A and 3B show the mass spectra for an injection of Alprazolam in a liquid stream flowing at 1 milliliter per minute (ml/min) with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 4A and 4B show the mass spectra for an injection of codeine-d3 in a liquid stream flowing at 400 µl/min with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 5A and 5B show the mass spectra for an injection of codeine-d3 in a liquid stream flowing at 1 ml/min with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 6A and 6B show the mass spectra for an injection of acetaminophen in a liquid stream flowing at 400 µl/min flow with -5V DC offset and -15V DC offset applied to the second ion guide.

Figures 7A and 7B show the mass spectra for an injection of Ibuprofen in a liquid stream flowing at 400 µl/min with +5V DC offset and +15V DC offset applied to the second ion guide.

Figure 8 is a schematic view of a mass spectrometer system as in Figure 1 with a single quadrupole mass analyzer rather than a tandem mass analyzer or other suitable mass analyzer.

Description of Preferred Embodiments

Referring to Figure 1, an atmospheric pressure ion source in chamber 11 is interfaced to a tandem mass analyzer 12 via three vacuum pumping stages. The first stage 13 which has the highest pressure is evacuated by an oil-filled rotary vane vacuum pump 14. Other types of vacuum pumps may also be used for this stage, such as a diaphragm pump or scroll pump. A typical pressure for first stage 13 is between 1 and 2 Torr. The second and third stages 16 and 17 are separated by a lens 18 with an orifice 19, which in one example was 1.5 mm in diameter, and can be evacuated by a hybrid or compound turbomolecular pump 21 which includes both turbomolecular and molecular drag pumping stages, and may have multiple inlets into each of these pumping stages, or by individual vacuum pumps (not shown). As will be explained in accordance with the present invention, the pressure in chamber 16 is below 500 mTorr, preferably below 250 mTorr, and more preferably below 175 mTorr; and the pressure in chamber 17 is below 1 mTorr, preferably below 0.7 mTorr, and more preferably below 0.5 mTorr. The pressure in the tandem mass analyzer chamber is approximately 1 x 10^{-5} Torr or below.

The atmospheric pressure ion source may be an electrospray ion source or atmospheric pressure chemical ionization source. With either ion source, sample liquid is introduced into the chamber 11, which is at atmospheric pressure, and ionized. The ions are drawn through a capillary 22, which may be heated, into chamber 13. The end of the capillary is opposite a conical skimmer 24 which includes a central orifice or aperture 26. The skimmer separates the low pressure stage 13 from the lower pressure stage 16. A portion of the ion and gas flow is skimmed from the

free jet expansion leaving the capillary and enters the second lower pressure stage. The ions which travel through the skimmer are guided into the mass analyzer by first and second multipole ion guides 27 and 28. In one example, the ion guides are square quadrupoles. The guide 27 is 1.25 inches long and the guide 28 is 3.37 inches with the rods separated by 0.118 inches (3 mm). The ion guides are mounted coaxially using polycarbonate holders (not shown). The quadrupole ion guides are operated by applying AC voltages 31 and 32 to the poles which guide ions as is well known. Ions which enter the second and third stages drift under the influence of DC voltage 33 applied between the skimmer lens 24 and lens 18, by DC voltage 34 applied between the lens 18 and the lens 36, and by DC offset voltages applied to ion guides 27 and 28.

As discussed above, solvent adduct ions are formed in the high pressure regions ranging from the atmospheric pressure region to the quadrupole ion guide stages or regions. The degree of adduction is believed to vary directly with the pressure in these regions. The formation of adduct ions can significantly reduce the abundance of sample analyte ions which reach the analyzer. Consequently, effective conversion of the adduct ions into protonated molecular cations or molecular anions ions can greatly enhance the sample ion current and the sensitivity of the mass spectrometer system.

We have discovered that the solvent adduct ions can be dissociated and converted into sample ions in the second ion guide 28 by applying a small DC offset voltage between the ion guide 28 and the lens 18 to increase the energy of the solvent adduct ions. An additional 10 volts DC offset applied to the second ion guide (usually used with a standard 5 V DC offset) is sufficient to convert the solvent adducts into the protonated molecular cation or molecular anion for all compounds tested. In addition, this offset voltage is insufficient to cause fragmentation of the analyte ions at the pressure of the second stage.

Both pumping efficiency and solvent adduction were evaluated. The pumping requirement and vacuum condition on the double ion guide system were compared to a standard TSQ 7000 system sold by ThermoQuest Corporation under the same gas load conditions. Several different compounds including a) acetaminophen; b) Alprazolam; c) codeine-d3; d) ibuprofen were used to investigate the degree of solvent adduction, conversion to protonated molecular cation or molecular anion, and fragmentation of the protonated molecular cation or molecular anion. The solvent

used in the experiment was 50:50 acetonitrile:water + 5mM ammonium acetate adjusted to a pH of 4.5. Table 1 lists the main experimental conditions, compound, molecular weight and type of solvent adduction investigated.

TABLE 1

Compound	Molecular Weight	Solvent Adduct	Ion Polarity	LC Flow (µl/min)	Sample Injected (ng)
Acetaminophen	151	Acetonitrile	Positive	400	500
Alprazolam	308	Acetonitrile	Positive	400 - 1000	1.6
Codeine-d3	302	Acetonitrile	Positive	400 - 1000	50
Ibuprofen	206	Acetate	Negative	200	50

Figures 2-7 show the comparative mass spectra for the four different compounds used in the evaluation under standard (±5 V DC) offset and an incremental 10 V DC (±15 V DC total) offset conditions between the interstage ion lens 18 and the second multipole ion guide 28 indicating that the signal intensity and peak area for the protonated molecular cations or molecular anions can be significantly enhanced by the application of the increased DC offset on the second multipole ion guide 28.

Figure 2A shows the mass scan for Alprazolam at 400 µl/min liquid chromatograph flow with the standard -5 volt offset, and Figure 2B shows Alprazolam with an incremental 10 volts of offset at the same flow rate. The increased sample ion signal produced by the incremental offset voltage is apparent.

Figures 3A and 3B show the mass spectra for Alprazolam at 1 ml/min flow. Again the increased sample ion current is apparent. Figures 4A and 4B show the mass spectra for codeine-d3 at 400 µl/min flow with the standard and increased offset voltages. The increased sample ion signal at *m/z* 302 is apparent. The same mass spectra are shown for 1 ml/min codeine-d3 in Figures 5A and 5B. Figures 6A and 6B show a comparison of the mass spectra for Acetaminophen at 400 µl/min flow with the standard and increased offset voltages. Again, the vast improvement in sensitivity is apparent. Figures 7A and 7B show the mass spectra for ibuprofen flowing at 400 µl/min flow with the standard and increased offset voltages. The improved signal at *m/z* 205 should be noted.

The DC offset required for high efficiency solvent adduct ion conversion at different vacuum conditions in both first chamber and second chamber was also investigated. The following tables summarize one set of tests in which the ratio of the acetonitrile adduct to the protonated molecular cation of codeine-d3 was investigated at different pressures and different DC offset voltages on the second ion guide.

TABLE 2

DC offset on second ion guide (volts)	-5	-5	-5	-5	-5
First ion guide pressure (mTorr)	609	563	502	224	167
Second ion guide pressure (mTorr)	1.6	1.2	1	0.7	0.5
Ratio of acetonitrile adduct ion to protonated molecular ion	704%	926%	288%	354%	248%

DC offset on second ion guide (volts)	-15	-15	-15	-15	-15
First ion guide pressure (mTorr)	609	563	**502**	**224**	**167**
Second ion guide pressure (mTorr)	1.6	1.2	**1**	**0.7**	**0.5**
Ratio of acetonitrile adduct ion to protonated molecular ion	445%	407%	**82%**	**38%**	**17%**

DC offset on second ion guide (volts)	-35	-35	-35	-35	-35
First ion guide pressure (mTorr)	609	563	**502**	**224**	**167**
Second ion guide pressure (mTorr)	1.6	1.2	**1**	**0.7**	**0.5**
Ratio of acetonitrile adduct ion to protonated molecular ion	300%	248%	**40%**	**7%**	**3%**

The bold data in Table 2 indicates the range of pressure and offset voltages at which the most efficient conversion of solvent adduct to protonated molecular cation is achieved. According to these results, the operating pressure for the ion guides should be:

First Ion Guide: below 500 mTorr

Second Ion Guide: below 1 mTorr and above 0.1 mTorr

Although the offset voltage which provides the translational kinetic energy to the adduct ions has been described as applied between the interstage lens and the second multipole guide, it is apparent that the translational kinetic energy can be

provided by applying the DC offset voltage between the skimmer lens and the first multipole stage or by applying voltages simultaneously between each lens and its respective multipole ion guide. The operating pressure will be the same as above.

The DC offset voltage range for efficient solvent adduction conversion should be ±10 to ±30 Volts, although ±10 V is preferable.

The preferred pressure range is less than 250 mTorr for the first stage and 0.7 mTorr for the second stage, and the most preferred pressure range is less than 175 mTorr for the first stage, and 0.5 mTorr for the second stage.

The present invention can be used for other types of mass analyzers such as quadrupole mass analyzers of the type described in U.S. Patent Nos. 4,540,884 and RE 34,000. Figure 8 shows the interface stages and ion guides associated with a quadrupole mass analyzer 41 disposed in the vacuum chamber 12. Like members have been applied to the parts which correspond to those in Figure 1. It is apparent that the invention is applicable to other types of mass analyzers such as quadrupole ion trap, ion cyclotron resonance (i.e., magnetic ion trap), time-of-flight, magnetic sector, and double-focusing magnetic/electric sector, monopole, etc.

What is Claimed is:

1. A mass spectrometer system including a mass analyzer disposed in a high vacuum chamber for analyzing ions formed at atmospheric pressure and directed to the analyzer through intermediate vacuum chambers including:

first and second evacuated chambers directly preceding the mass analyzer chamber with the first chamber being at a higher pressure than the second chamber,

a first multipole ion guide in the first chamber for guiding ions into said second chamber,

a second multipole ion guide in the second chamber for guiding ions from the first chamber into the high vacuum chamber for mass analysis, and

means associated with one or both of said first and second multipole ion guides for increasing the translational kinetic energy of the adduct ions so that at the vacuum pressure of the second interface chamber adduct ions traveling into the chamber are converted into protonated molecular cations or molecular anions ions without fragmentation of these ions whereby to increase the sample ion current and therefore the sensitivity of the mass spectrometer system.

2. A mass analyzer as in claim 1 including ion lenses preceding each said multipole ion guide and a DC voltage is applied between a selected lens and its associated ion guide to increase the translational kinetic energy of the adduct ions entering the second interface chamber.

3. A method of mass analyzing ions produced at atmospheric pressure, in which adduct ions are formed, and introduced into a mass analyzer disposed in a vacuum chamber,

the step of dissociating the adduct ions prior to entry into the mass analyzer to increase the analyte ion current into the mass analyzer.

4. The method of operating a mass spectrometer system including a mass analyzer which analyzes ions formed at atmospheric pressure, said system including

first and second multipole ion guides disposed in serial first and second evacuated chambers separated by an ion lens for guiding analyte ions into said mass analyzer and an ion lens defining the first evacuated chamber which comprises

applying a DC offset voltage between a selected one or both ion lenses and the succeeding multipole ion guide having an amplitude so as to provide translational kinetic energy to said adduct ions to dissociate the adduct ions at the pressure of the second chamber to increase the sample ion current and the sensitivity of the mass spectrometer system.

5. A mass spectrometer system as in claim 4 in which the pressure in the first chamber is below 500 mTorr, and in the second chamber is below 1 mTorr, and the offset voltage applied between the interchamber lens and the second multipole ion guide is between ±10 volts and ±30 volts.

6. A mass spectrometer system as in claim 5 in which the pressure in the first chamber is less than 250 mTorr, and in the second chamber is less than 0.7 mTorr.

7. A mass spectrometer system as in claim 5 in which the pressure in the first chamber is less than 175 mTorr, and in the second chamber is less than 0.5 mTorr.

8. A mass spectrometer as in claim 6 or 7 in which the offset voltage is ±10 volts.

9. The method of analyzing ions and adduct ions produced at or near atmospheric pressure in a mass analyzer,

guiding said ions and adduct ions through at least a first chamber maintained at a first pressure and a second chamber maintained at a lower pressure,

adding translational kinetic energy to said adduct ions as they travel through said chambers such that in the second chamber the adduct ions are dissociated prior to entering the mass analyzer.

ABSTRACT

There is described an interface for delivering ions generated in an ion source into a mass analyzer in a chamber under vacuum pressure. In particular, the interface employs two consecutive ion guides operated to dissociate adduct ions formed in the ion source or high pressure regions of the interface between the ion source and the mass analyzer, thus improving the limit of detection or limit of quantitation of the mass analyzer by increasing the analyte ion current.

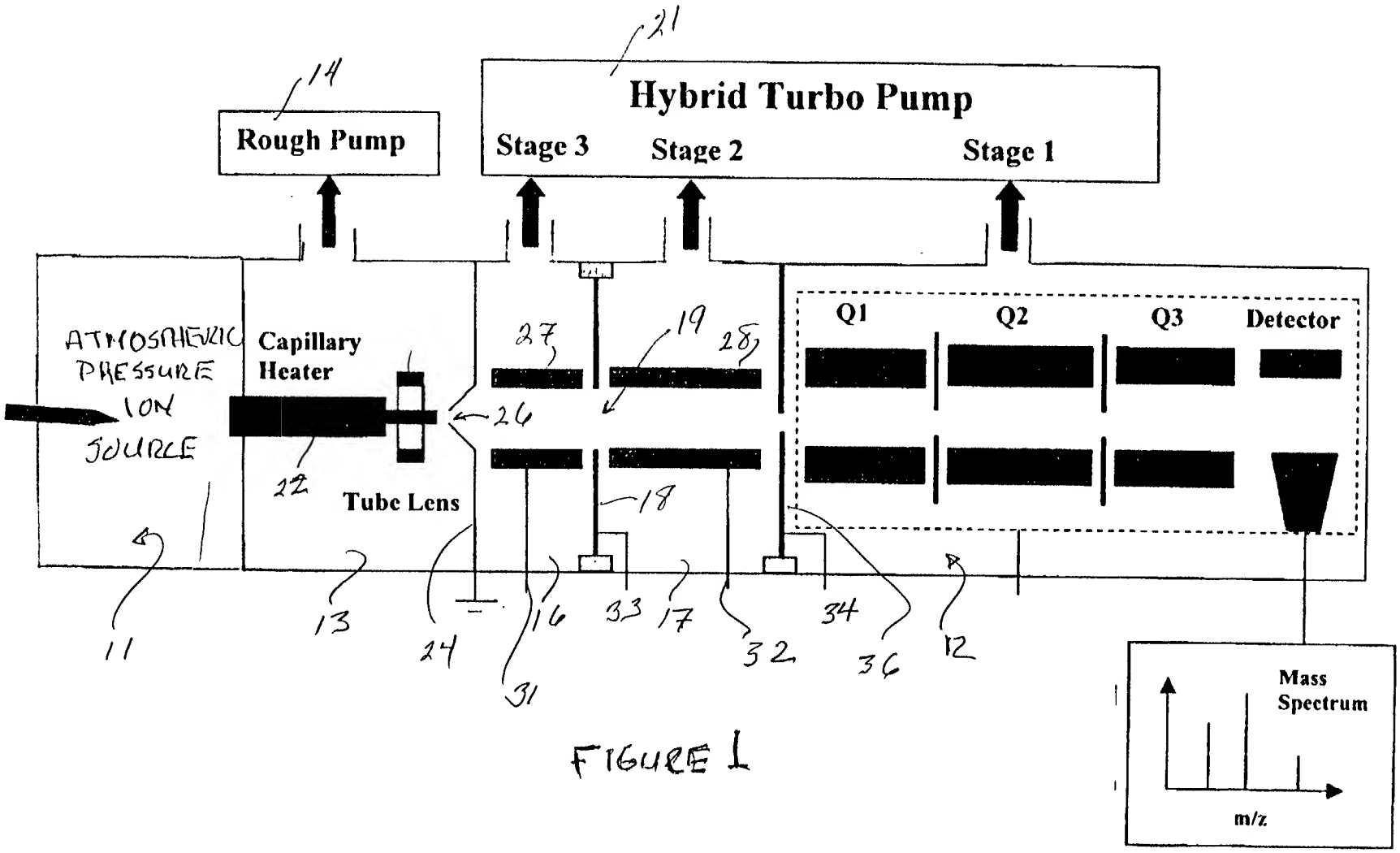
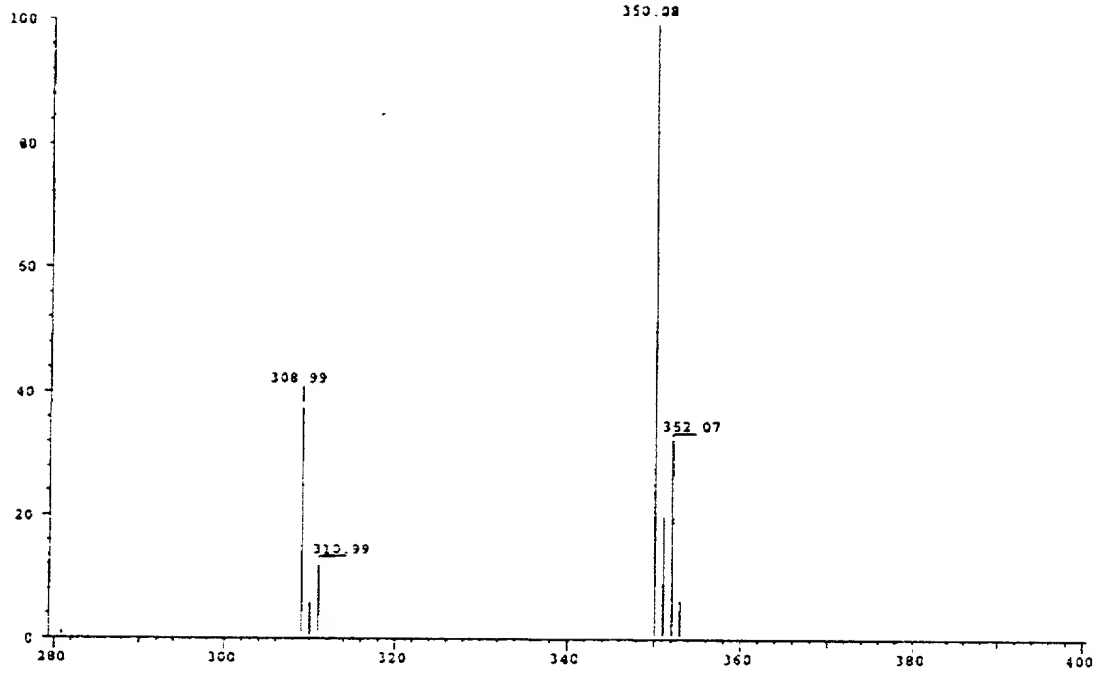

21
14
Rough Pump
Hybrid Turbo Pump
Stage 3
Stage 2
Stage 1
ATMOSPHERIC PRESSURE ION SOURCE
Capillary Heater
Tube Lens
Q1
Q2
Q3
Detector
27
19
28
26
22
18
11
13
24
31
16
33
17
32
34
36
12
Mass Spectrum
m/z

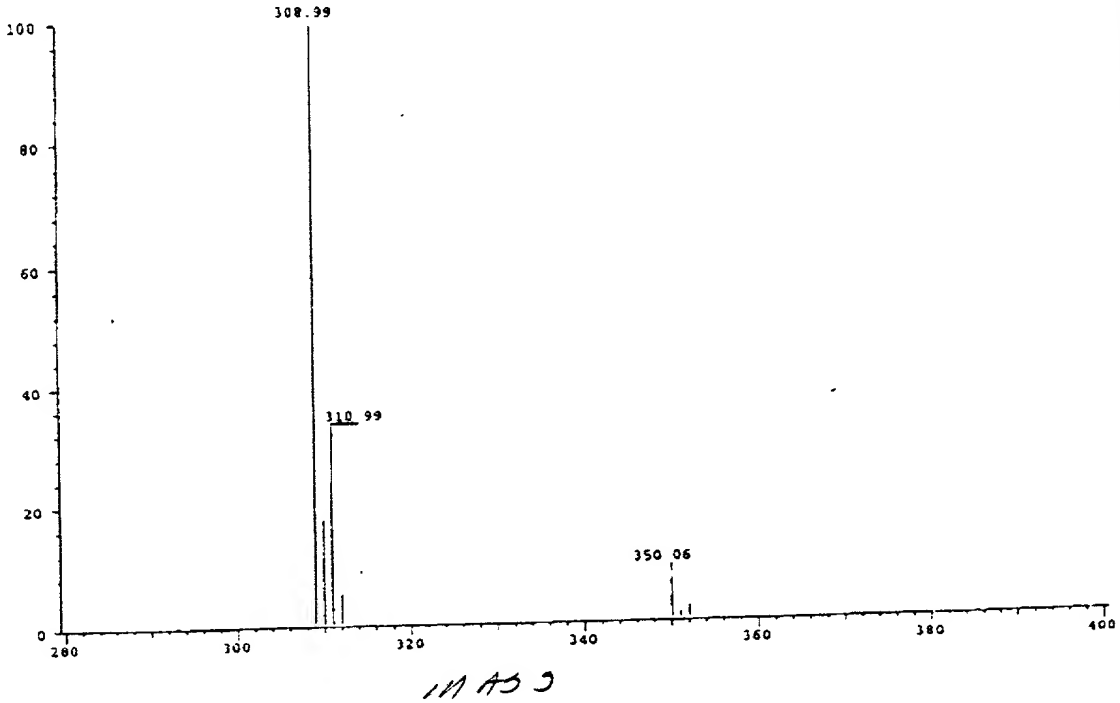
FIGURE 1



Intensity

MASS

FIGURE 2A



Intensity

MASS

FIGURE 2B

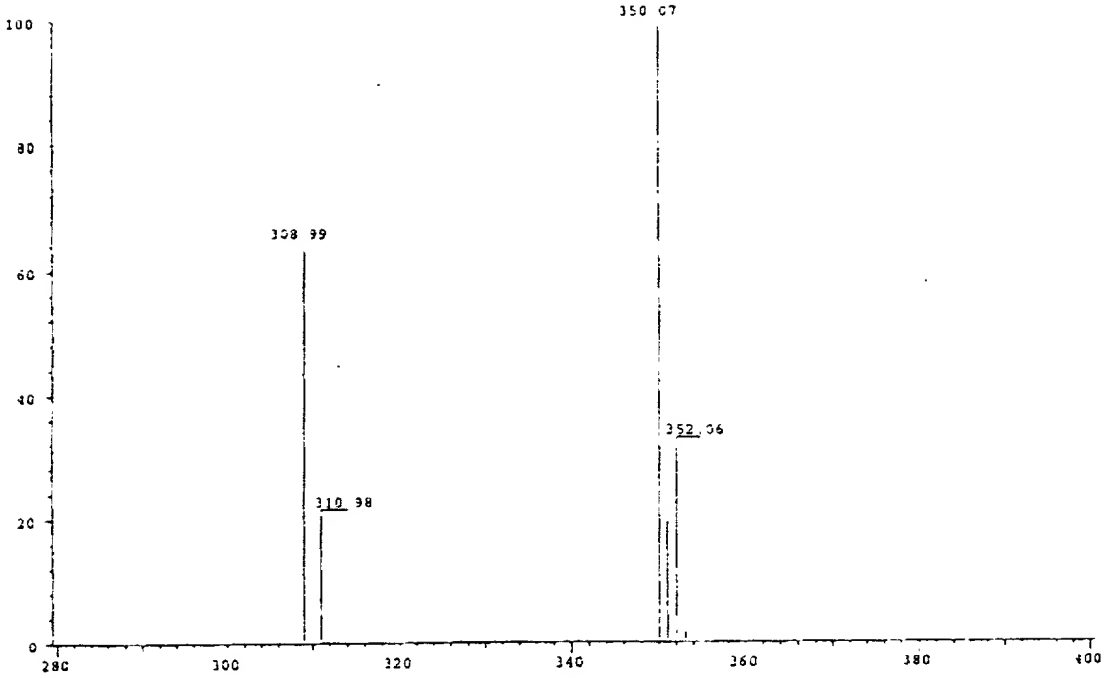


FIGURE 3A

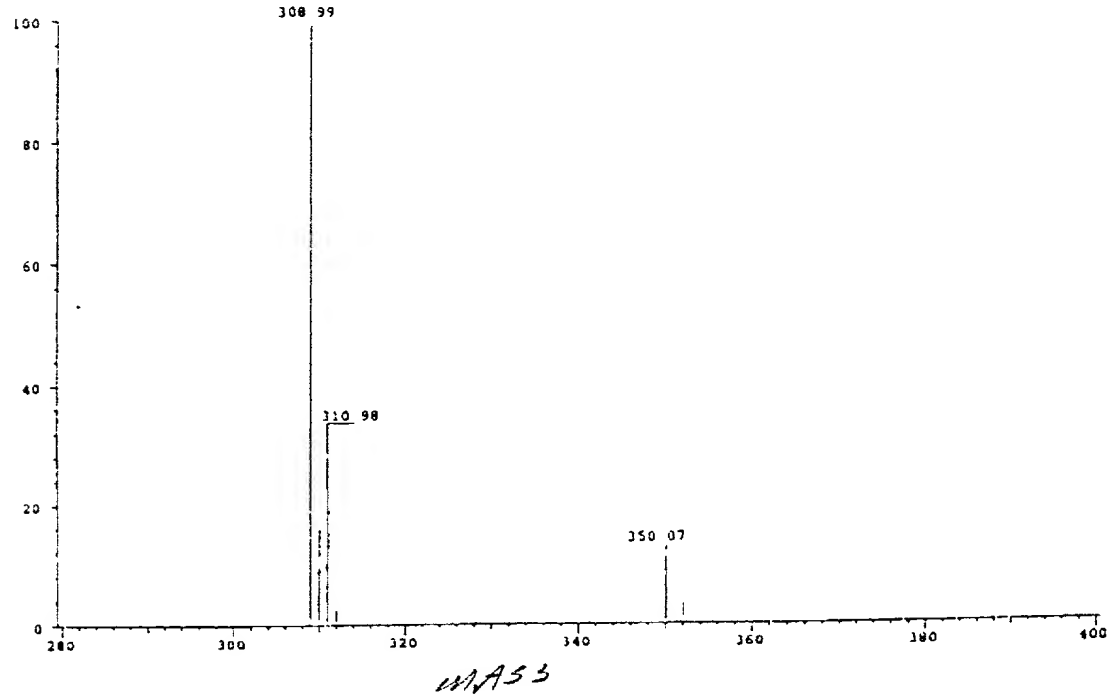
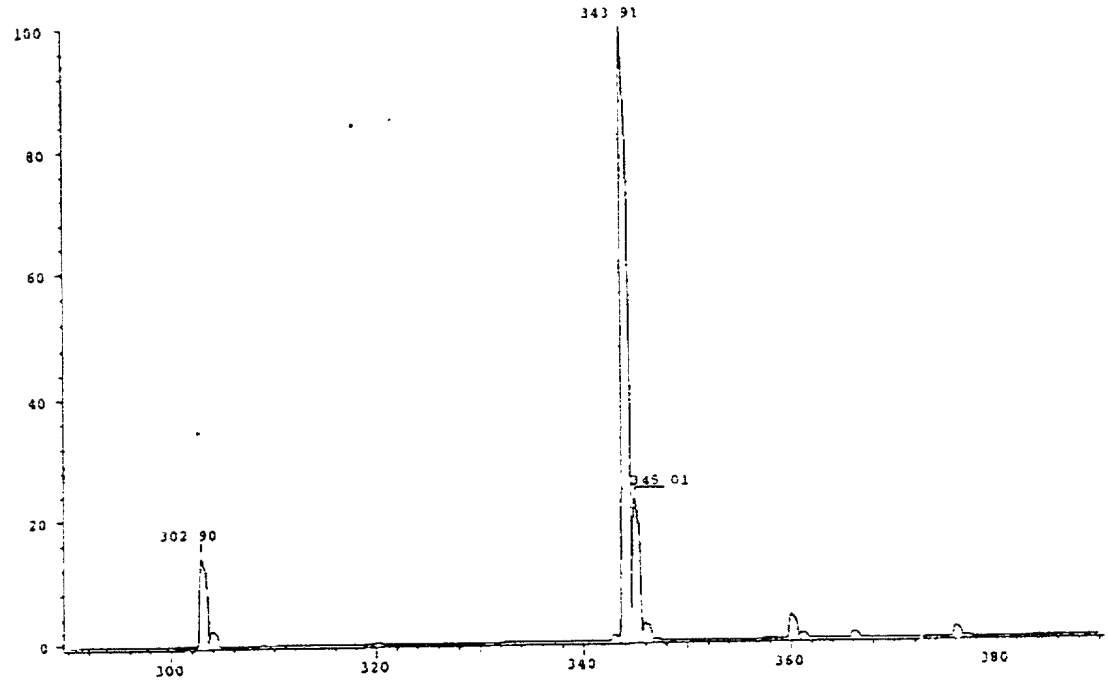


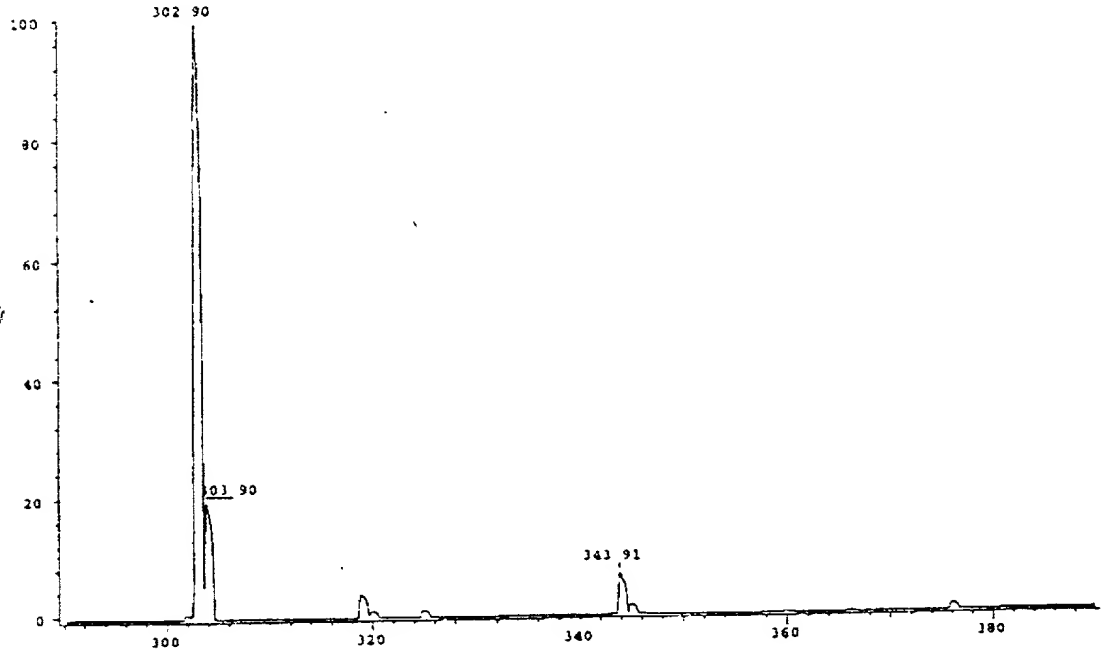
FIGURE 3B.



Intensity

MASS

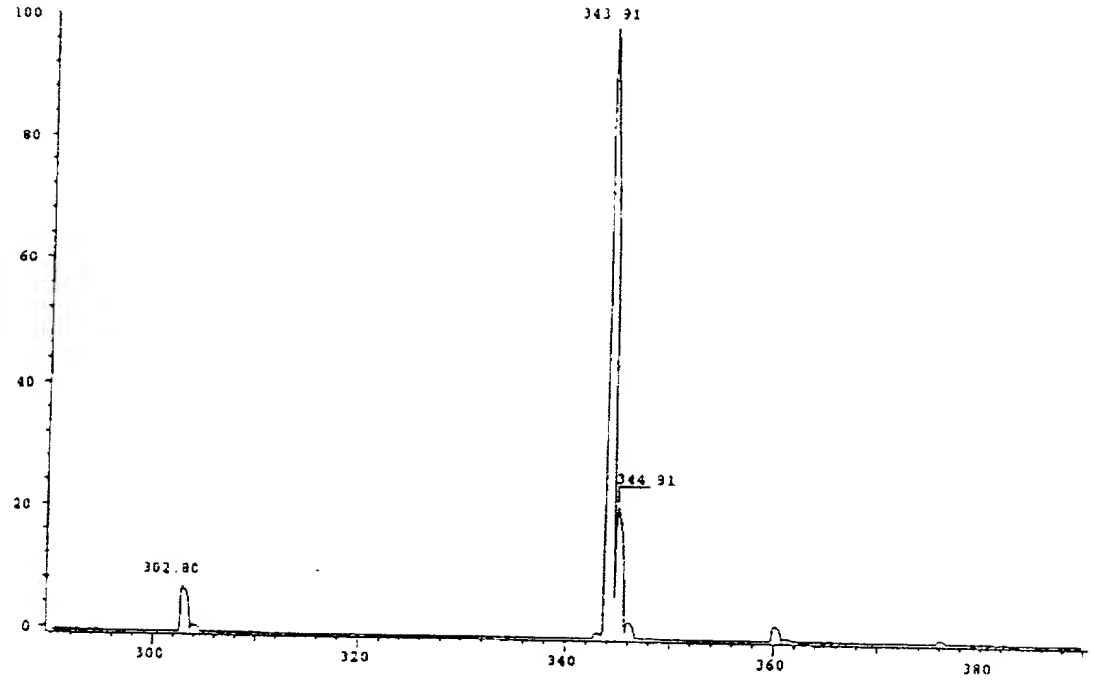
FIGURE 4A



Intensity

MASS

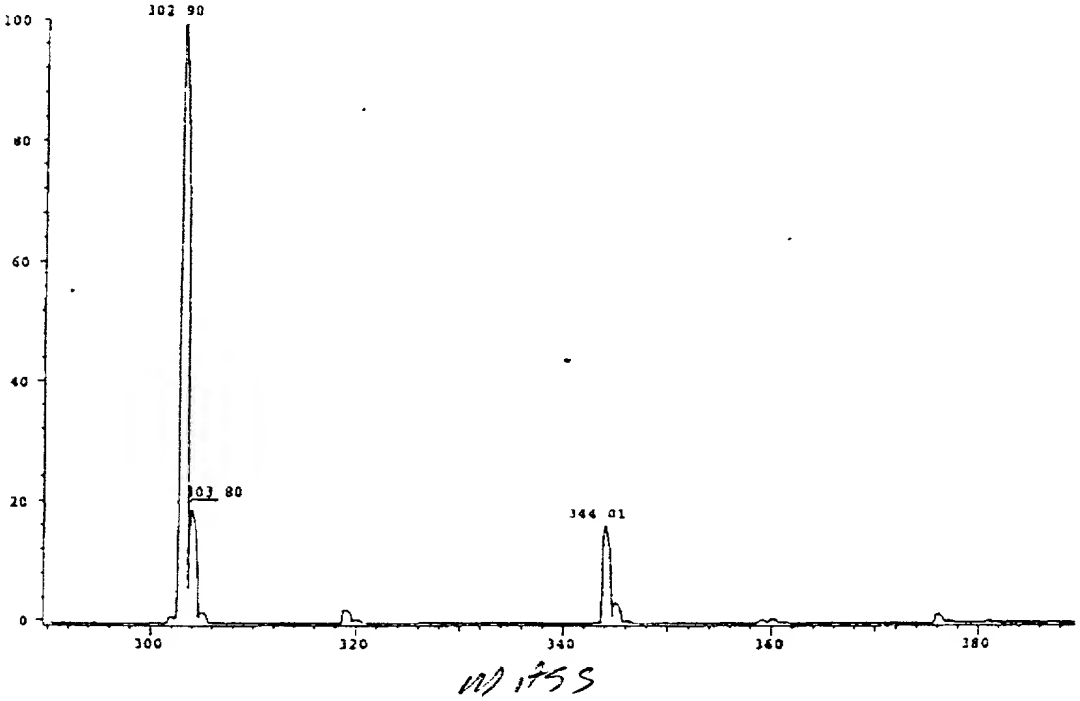
FIGURE 4B



Intensity

FIGURE 5A

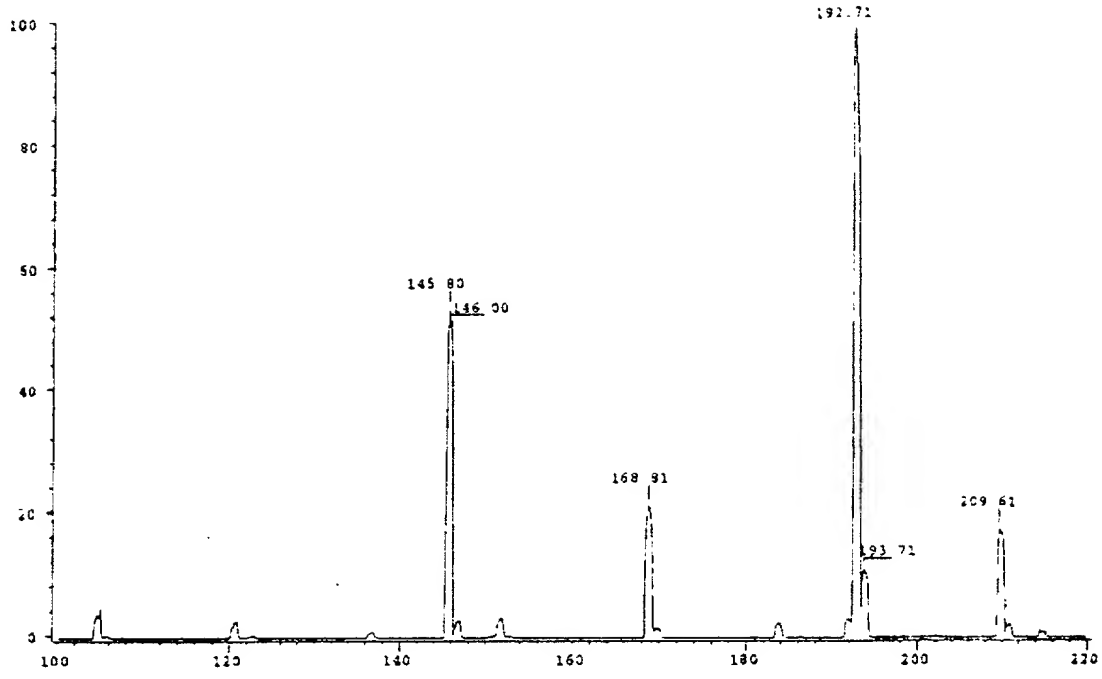
MASS



Intensity

MASS

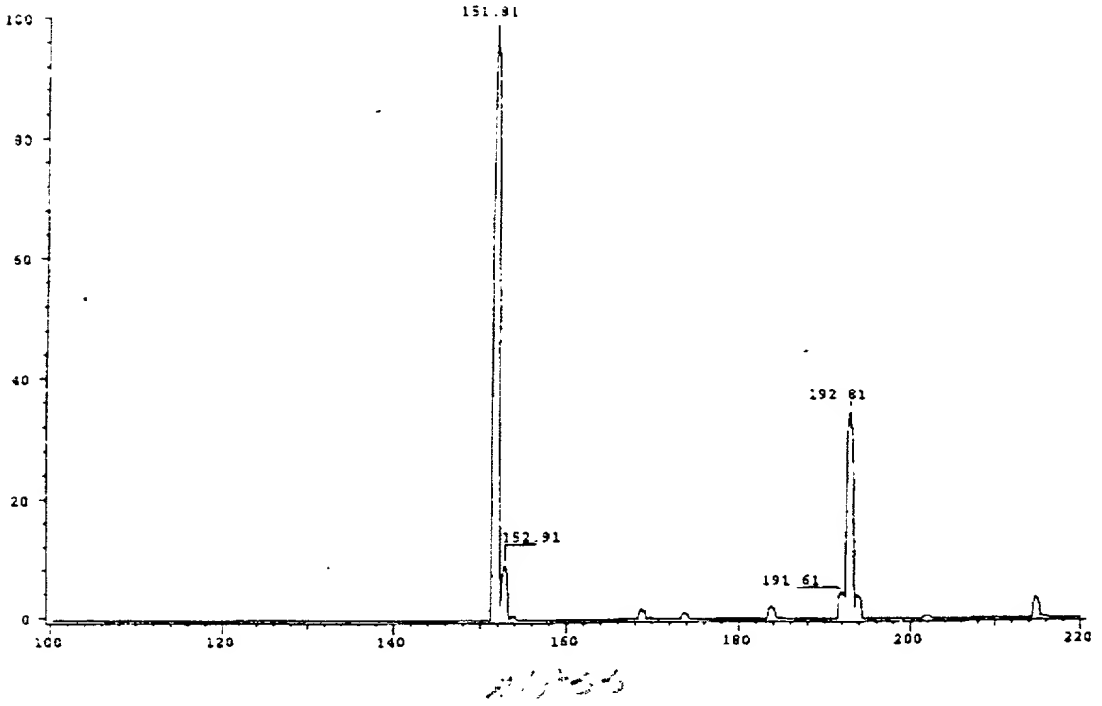
FIGURE 5B



Intensity

m/z

FIGURE 6A



Intensity

m/z

FIGURE 6B

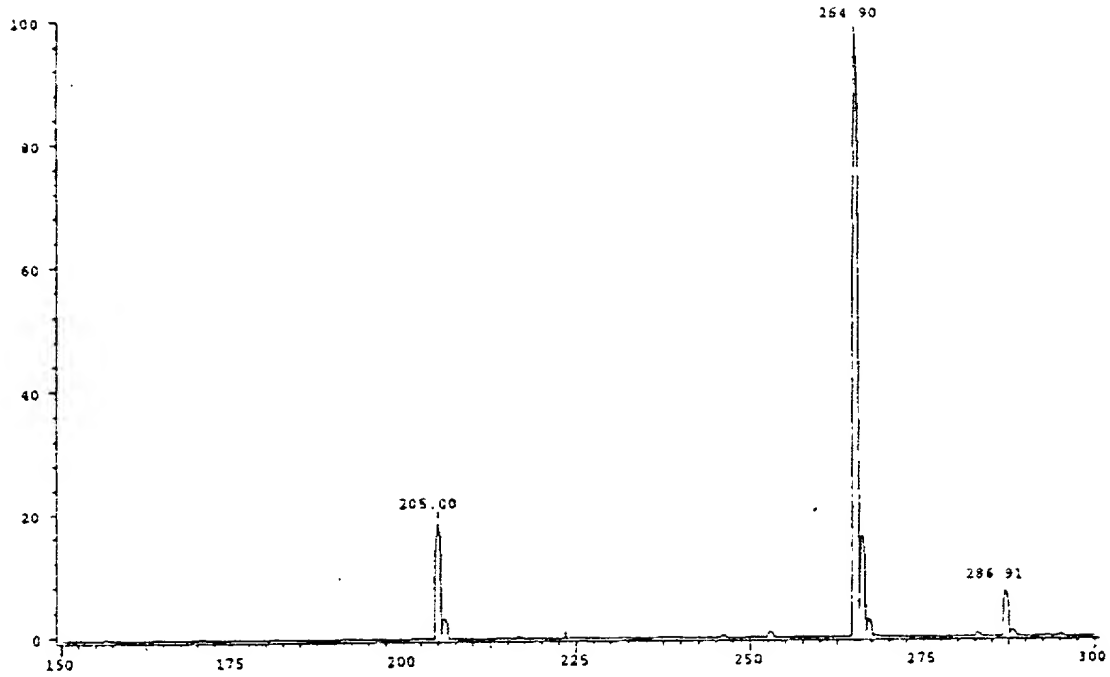


FIGURE 7A

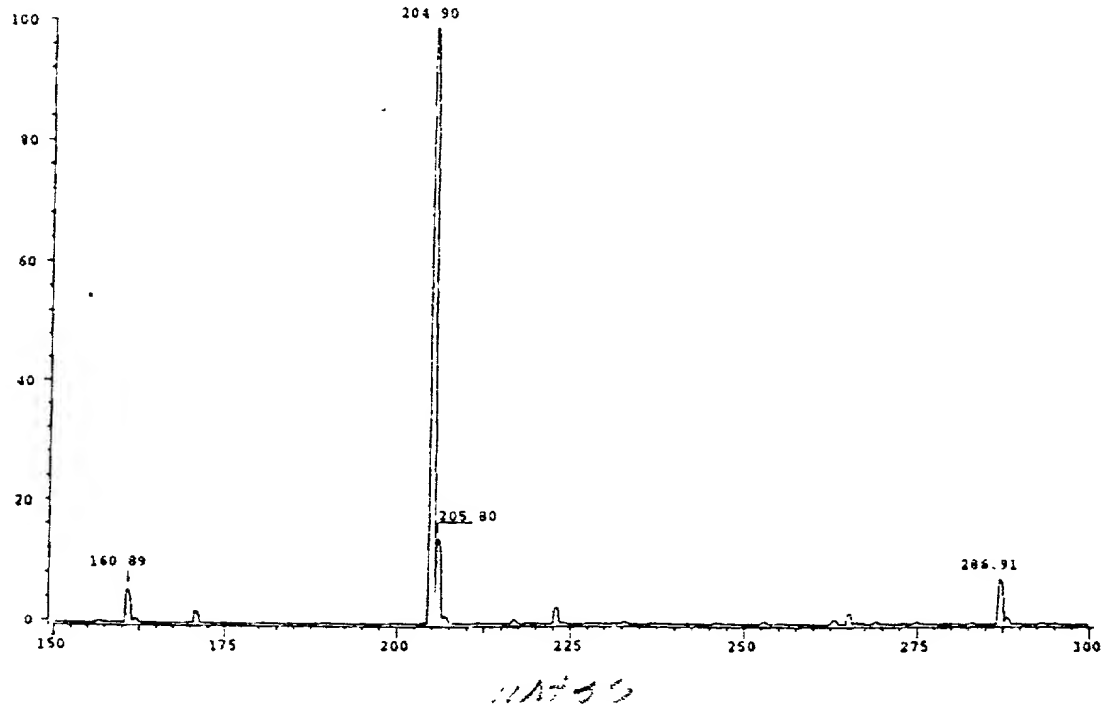


FIGURE 7B

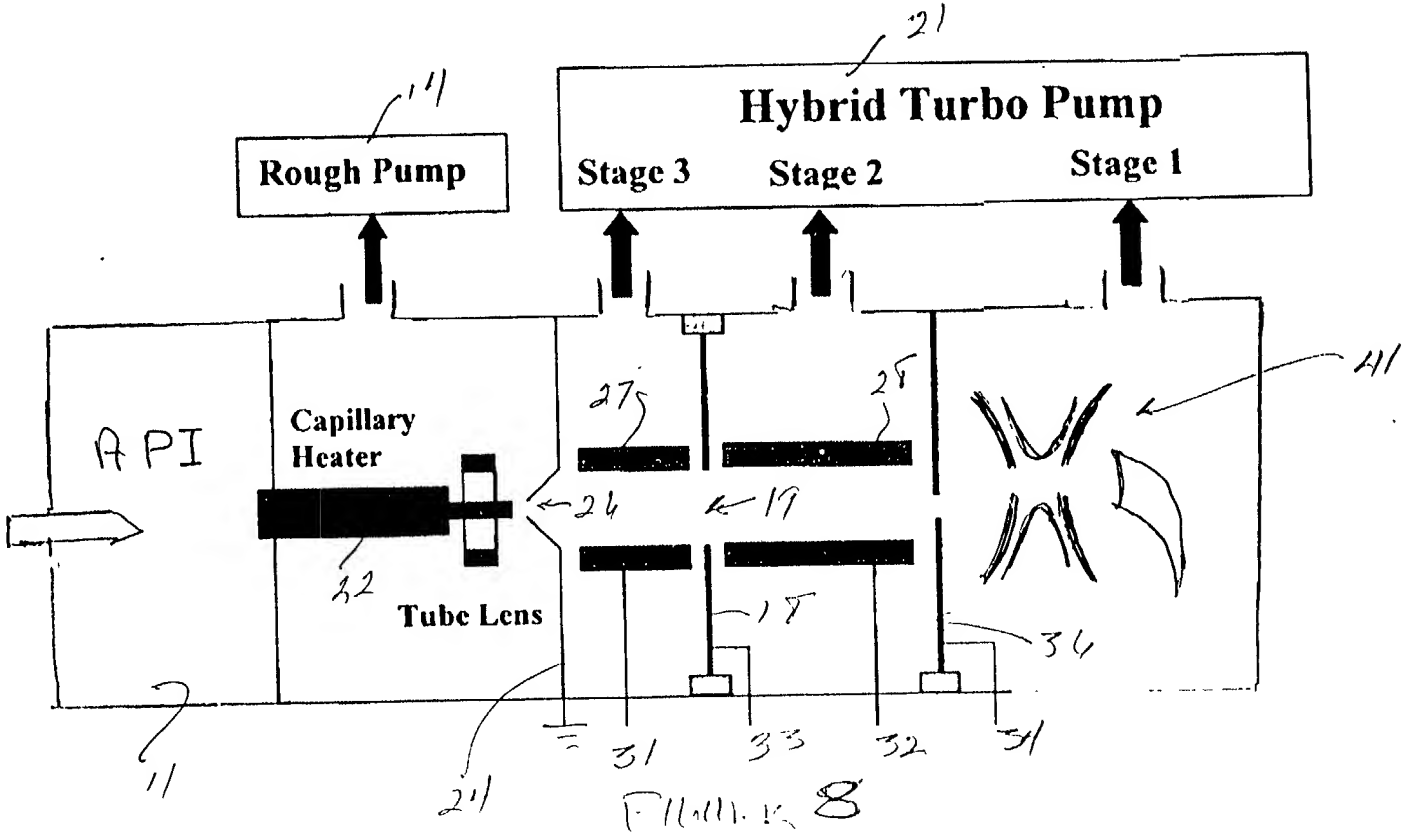

21
Hybrid Turbo Pump
Stage 3
Stage 2
Stage 1
14
Rough Pump
API
Capillary
Heater
22
Tube Lens
27
25
24
17
18
41
36
11
21
31
33
32
31

FIG. 8

DECLARATION FOR PATENT APPLICATION

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled MASS SPECTROMETER SYSTEM INCLUDING A DOUBLE ION GUIDE INTERFACE AND METHOD OF OPERATION,

the specification of which

(check one)

[X] is attached hereto.

[ ] was filed on _____ as Application Serial No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
			[ ]	[ ]
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No
			[ ]	[ ]
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No
			[ ]	[ ]
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

09/454,273	December 3, 1999	pending
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

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File No. A-67824-1/AJT

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, United States Code, §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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